

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (currently amended) An *in vitro* method A research model for screening compounds suspected of modulating that modulate the CD40L/CD40R signaling pathway by interfering with the CD40L/CD40R signaling pathway in an animal, human, or system, said method comprising the following steps:
 - (i) contacting a first sample of neuronal cells that express CD40R with CD40 ligand and measuring the level or amount of a marker one or more markers;
 - (ii) contacting a second sample of said neuronal cells with a compound and CD40 ligand and measuring the level or amount of a marker said one or more markers; and
 - (iii) comparing the level or amount of the marker said one or more markers of the first sample of cells determined in step (i) with the level or amount of the marker said one or more markers of the second sample of cells determined in step (ii), wherein a difference in the levels or amounts of the said one or more markers measured in steps (i) and (ii) indicates a compound that modulates the CD40L/CD40R signaling pathway.
2. (canceled)
3. (currently amended) The method of claim 1, wherein the marker said one or more markers is the levels or amounts level or amount of one or more cytokines.
4. (currently amended) The method of claim 3, wherein the cytokine said one or more cytokines is selected from the group consisting of tumor necrosis factor, interleukin 1, interleukin 6, interleukin 12, interleukin 18, macrophage inflammatory protein, macrophage chemoattractant protein, granulocyte-macrophage colony stimulating factor, and macrophage colony stimulating factor, and combinations thereof.

5. (withdrawn) The method of claim 1, wherein ~~the marker said one or more markers~~ is selected from ~~the group consisting of levels, amounts or activities~~ ~~the level amount or activity~~ of glutamate release, nitric oxide production, nitric oxide synthase, superoxide, or superoxide dismutase, ~~glutamate release, nitric oxide production, nitric oxide synthase, superoxide, and superoxide dismutase, and combinations thereof.~~
6. (withdrawn) The method of claim 1, wherein ~~the marker said one or more markers~~ is selected from ~~the group consisting of~~ a major histocompatibility complex molecule, CD45, CD11b, F4/80 antigen, integrins, ~~or~~ a cell surface molecule, and combinations thereof.
7. (withdrawn) The method of claim 1, wherein ~~the marker said one or more markers~~ is ~~one or more of decreased neuronal inflammation,~~ the levels or amounts of A β , β -amyloid precursor protein (β -APP), a fragment ~~fragments~~ of β -APP, ~~or fragments a~~ fragment of A β , or combinations thereof.

8-92. (canceled)

93. (new) The method of claim 1, wherein said compound is a compound that modulates the CD40L/CD40R signaling pathway upstream or downstream of CD40L/CD40R interaction.
94. (new) The method of claim 93, wherein said compound binds to CD40R, binds to CD40L, or interferes with TNF receptor-associated factors.
95. (new) The method of claim 94, wherein said compound binds to CD40R and decreases trimerization of CD40R.
96. (new) The method of claim 94, wherein said compound binds to CD40L and decreases trimerization of CD40L.
97. (new) The method of claim 1, wherein said compound alters APP processing.
98. (new) The method of claim 97, wherein said compound modulates presenilin-1 activity, modulates presenilin-2 activity, inhibits β -secretase activity, inhibits γ -secretase activity, or enhances α -secretase activity.

99. (new) The method of claim 93 or 97, wherein said compound reduces the ratio of APP β -CTF to APP α -CTF, reduces the amount or level of β -CTF, reduces soluble β -amyloid levels, or reduces total β -amyloid levels relative to a control culture.

100. (new) The method of claim 1, 93 or 97, wherein said compound is a soluble CD40R compound or variant thereof, or a soluble CD40L compound or variant thereof.

101. (new) The method of claim 100 wherein said compound is a soluble CD40L compound or variant thereof, which compound is immunogenic.

102. (new) The method of claim 1, 93 or 97, wherein said compound is an interfering or antisense RNA compound to CD40R or CD40L.

103. (new) The method of claim 102 wherein said compound is an interfering RNA compound, which compound is dsRNA, RNAi or siRNA.

104. (new) The method of claim 1, 93, or 97, wherein said compound is an antibody to CD40R.

105. (new) The method of 104, wherein said antibody agonizes CD40R activity.

106. (new) The method of claim 104, wherein said antibody antagonizes CD40R activity.

107. (new) The method of claim 1, 93, or 97, wherein said compound is an antibody to CD40L.

108. (new) The method of 107, wherein said antibody agonizes CD40L activity.

109. (new) The method of claim 107, wherein said antibody antagonizes CD40L activity.

110. (new) The method of claim 1, wherein said neuronal cells are neurons or neuroblastoma cells.

111. (new) The method of claim 110, wherein said cells are neuroblastoma cells, which cells are N2a cells.

112. (new) The method of claim 1, wherein said neuronal cells are derived from a transgenic animal.

113. (new) The method of claim 112, wherein the transgenic animal expresses transgenic APP or expresses transgenic tau protein.

114. (new) The method of claim 112, wherein the transgenic animal overexpresses presenilin protein, overexpresses CD40R, or overexpresses CD40L.

115. (new) The method of claim 1, wherein said neuronal cells are derived from an animal afflicted with a disease or disorder associated with neuronal inflammation.

116. (new) The method of claim 115, wherein said disease or disorder is an amyloidogenic disease.

117. (new) The method of claim 1, wherein said neuronal cells are derived from an animal afflicted with an amyloidogenic disease.

118. (new) The method of claim 116 or 117, wherein said amyloidogenic disease is Alzheimer's disease, scrapie, transmissible spongiform encephalopathy, hereditary cerebral hemorrhage with amyloidosis Icelandic-type, hereditary cerebral hemorrhage with amyloidosis Dutch-type, familial Mediterranean fever, familial amyloid nephropathy with urticaria and deafness (Muckle-Wells syndrome), myeloma or macroglobulinemia-associated idiopathy associated with amyloid, familial amyloid polyneuropathy (Portuguese), familial amyloid cardiomyopathy (Danish), systemic senile amyloidosis, familial amyloid polyneuropathy (Iowa), familial amyloidosis (Finnish), Gerstmann-Staussler-Scheinker syndrome, medullary carcinoma of thyroid, isolated atrial amyloid, diabetes Type II, or insulinoma.

119. (new) The method of claim 116 or 117, wherein the amyloidogenic disease is a tauopathy.

120. (new) The method of claim 116, wherein said tauopathy is Alzheimer's disease, frontotemporal dementia, frontotemporal dementia with Parkinsonism, frontotemporal lobe dementia, pallidopontonigral degeneration, progressive supranuclear palsy, multiple system tauopathy, multiple system tauopathy with presenile dementia, Wilhelmsen-Lynch

disease, disinhibition-dementia-parkinsonism-amyoatrophy complex, Pick's disease, or Pick's disease-like dementia.